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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,653	03/23/2001	Diane Pennica	10716-57/CURA233/GNI885R1	6857

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EXAMINER

NICKOL, GARY B

ART UNIT PAPER NUMBER

1642

DATE MAILED: 03/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/816,653

Applicant(s)

PENNICA ET AL.

Examiner

Gary B. Nickol Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 and 33-35 is/are pending in the application.
- 4a) Of the above claim(s) 5-31 and 33-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15-16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The Election filed November 7, 2002 (Paper No. 14) in response to the Office Action of July 2, 2002 is acknowledged and has been entered.

Claims 1-31, 33-35 are pending in the application.

Claims 5-31, 33-35 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-4 are currently under prosecution

Applicant's election with traverse of Group I, Claims 1-4 in Paper No 14 is acknowledged. The traversal is on the ground(s) that the inventions have not been shown to be independent because the Office has simply state a conclusion without support, and that the examination of all groups would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in Paper No. 11. As to the question of burden of search, the inventions are classified differently, necessitating different searches in the literature. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The disclosed utilities for the hSTRA6 polypeptides comprising 80%, 90% or 98% identity to the sequence of one or both of SEQ ID NOs:2 and 4 and active polypeptides thereof include therapies directed to treating tumors, such as breast and colon tumors (page 15, line 5), screening methods to identify modulators of hSTRA6 expression (page 66, lines 25+), and diagnostic assays for determining hSTRA6 activity in the context of a biological sample such as blood, serum, cells, and tissue to determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant hSTRA6 activity, including cancer (page 69, lines 1+). However, neither the specification nor any art of record teaches what the hSTRA6 is, how it functions, or a specific and well-established utility for any of the polypeptides claimed. Furthermore, the specification does not teach a relationship to any specific disease or establish any involvement in the etiology of any specific disease. The asserted utility of the hSTRA6 polypeptides appears to be based on the assertion that hSTRA6 (i.e. SEQ ID NO:2 and or 4) is structurally similar to the mSTRA6 polypeptide (murine) as set forth in Table 5, page 14 and also has some structural similarity to synaptophorin, members of the G-protein coupled receptor family, and the tumor necrosis factor receptor (page 14). Further, the specification teaches that hSTRA6 is up-regulated in Wnt-1 expressing cells in-vitro (page 82), and that genes that are differentially regulated by Wnt-1 overexpression, when compared to wild-

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type or non-transforming Wnt-4 expressing cells, represent candidate genes that are involved in tumorigenic processes (page 1, line 30).

However, evidence based on protein sequence homology does not alone permit extrapolation to an isolated amino acid's biological function or use thereof. For example, Bowie *et al.* (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). The authors further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. This is because certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess *et al.* (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Further, Scott *et al.* (Nature Genetics, 1999, 21:440-443) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport

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proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter 'downregulated in adenoma'. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. The authors suggest that these results underscore the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph). Hence, these references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Thus, despite the asserted homology between mSTRA6 and hSTRA6, and despite the apparent increase in expression in Wnt-1 expressing cells, there are still large differences in the amino acid sequences and it cannot be predicted, based on the information in the specification, what affect this difference has on the function of the protein. Further, even if the polypeptide of SEQ ID NOs:2 and 4 are structurally similar to mSTRA6 polypeptides, neither the specification nor any art of record teaches what the polypeptide is, what it does, nor teach a relationship to any specific disease or establish any involvement of the polypeptides in the etiology of any specific disease or teach which polypeptides might be active.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptides. Thus, because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

If applicant were able to overcome the rejections under 35 USC 101 and USC 112 1st paragraph above, the following claims would still be rejected:

Claims 1-4 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NOs:2 and 4 and therefore the written description is not commensurate in scope with the claims drawn to naturally occurring amino acid sequences having at least 80% sequence identity to the sequence of SEQ ID NOs:2 and 4 wherein said polypeptide is an active hSTRA6 polypeptide and/or naturally occurring amino acid sequences having at least 90% or 98% sequence identity to the sequence of SEQ ID NOs:2 and 4.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlag, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined, nor in this case, is the structure of allelic variant proteins encoded by allelic variant genes defined. With the exception of SEQ ID NOs:2 and 4, the skilled artisan cannot envision the detailed structure of the encompassed amino acid sequences comprising 80%, 90% or 98% sequence identity to SEQ ID NOs:2 and 4, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these

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court findings are drawn to DNA art, the findings are clearly applicable to the claimed naturally occurring amino acid sequences.

Furthermore, although drawn specifically to the DNA art, the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’requires a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”.

Support for allelic variants is provided in the specification on page 21, lines 5+ where it is disclosed that DNA sequence polymorphisms that change the amino acid sequence of the hSTRA6 may exist within a population. For example, allelic variation among individuals will exhibit genetic polymorphism in hSTRA6. However, no disclosure, beyond the mere mention of allelic sequences is made in the specification. Further, there is no teaching of which fragments are biologically “active”. The specification only teaches (page 20) that an active hSTRA6 polypeptide or hSTRA6 polypeptide fragment retains a biological and or an immunological activity similar, but not necessarily identical, to an activity of a naturally-occurring (wild-type) hSTRA6 polypeptide of the invention, including mature forms. These teachings are insufficient to support the generic claims as set forth in the Written Description Guidelines.

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Therefore only an isolated polypeptide comprising the amino acids of SEQ ID NOs:2 or 4, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) **an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent** or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by any one of the following:

(1) Pennica *et al.* US Patent Application No: 20020156252A1, Prior Filing Date: 01-13-2000.

(2) Pennica *et al.* US Patent Application No: 20020173461A1, Prior Filing Date: 01-13-2000.

(3) Baker *et al.* US Patent Application No: 20030027988A1, Prior Filing Dates: 1997, 1998, 1999.

(4) Baker *et al.* US Patent Application No: 20030036635A1, Prior Filing Dates: 1997, 1998, 1999.

(5) Baker *et al.* US Patent Application No: 20030045687A1, Prior Filing Dates: 1997, 1998.

(6) Baker *et al.* US Patent Application No: 20030044934A1, Prior Filing Dates: 1997, 1998.

Each of the above references (see attached sequence comparisons at the end of this action) teach an isolated polypeptide comprising an amino acid sequence having at least 80%, at least 90%, or at least 98% sequence identity to SEQ ID NO:2 wherein said polypeptide is inherently an active hSTRA6 polypeptide.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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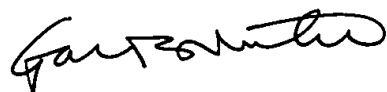
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Gary B. Nickol, Ph.D.
Examiner
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GBN

March 14, 2003

A handwritten signature in black ink, appearing to read "Gary B. Nickol". The signature is written in a cursive, flowing style with a large initial "G" and a long, sweeping underline.